UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,523	12/23/1999	Richard B. van Breemen	21726/90386	7519

23644 7590 03/23/2004

BARNES & THORNBURG
P.O. BOX 2786
CHICAGO, IL 60690-2786

EXAMINER	
TRAN, MY CHAU T	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/471,523	VAN BREEMEN ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-30* is/are pending in the application.

4a) Of the above claim(s) *24-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-23 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 December 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's amendment filed on 12/18/03 is acknowledged and entered. Claims 13 and 19 have been amended.

2. Applicant's response filed 12/8/03 and comments made during the interview have been considered. Note that the examiner's interview summary has been mailed on 12/16/03.

3. It is noted that applicants have not provided a formal statement of the substance of the interview according to MPEP section 713.04.

4. Claims 1-5, and 7-12 have been canceled by the amendment filed on 12/3/03.

5. Claim 6 has been canceled by the amendment filed on 3/5/02.

6. This application is a divisional of a PCT/US99/11,493 filed 5/25/1999, which claims priority to a provisional application 60/086,813 filed 5/26/1998.

7. Claims 13-30 are pending.

Election/Restrictions

8. This application contains claims 24-29, drawn to an invention nonelected with traverse in Paper filed 6/25/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Objections and /or Rejections

9. In view of applicant's amendment of claim 13, the previous rejection under 35 USC 112, first paragraph (written description), for claims 13-23, and 30 has been withdrawn.

10. In view of applicant's amendments of claims 13 and 19, the previous rejections under 35 USC 112, second paragraph, of claims 13-23, and 30 have been withdrawn.

11. In view of applicant's amendments of claims 13 and 19, the previous rejection of claims 13-21 under 35 U.S.C. 102(b) as anticipated by van Breemen et al. (*Analytical Chemistry*, **06/01/1997**, 69(11):2150-2164) has been withdrawn.

12. In view of applicant's amendments of claims 13 and 19, the previous rejection of claims 13-21 under 35 U.S.C. 102(b) as anticipated by Zhao et al. (*J. Med. Chem.*, **12/05/1997**, 40(25):4006-4012) has been withdrawn.

13. In view of applicant's amendments of claims 13 and 19, the previous rejection of claims 13-22 under 35 U.S.C. 102(b) as anticipated by Venton et al. (US Patent 5,366,862) has been withdrawn.

14. In view of applicant's amendments of claims 13 and 19, the previous rejection of claims 13-21, and 30 under 35 U.S.C. 102(e) as anticipated by Venton et al. (US Patent 5,872,015) has been withdrawn.

15. In view of applicant's amendments of claims 13 and 19, the previous rejection of claims 13-23, and 30 under 35 U.S.C. 103(a) as obvious over Venton et al. (US Patent 5,366,862) and Venton et al. (US Patent 5,872,015) has been withdrawn.

New Rejections – Necessitated by Amendment

Claim Rejections - 35 USC § 112

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 13-23, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a written description rejection)

The instant claim 13 recites a high throughput method for screening a compound of interest comprising the steps of 1) placing a solution of biological material that has a higher molecular weights than the compound of interest into an ultrafiltration chamber. The chamber comprises a membrane with a pore size that does not allow the biological material to pass through; 2) Placing the compound of interest into the ultrafiltration chamber, which comprises a membrane with a pore size that does allow passage of the compound; 3) Providing a continuous flow of a supportive solution to the ultrafiltration chamber that facilitates the reaction between the compound and biological material; 4) The product produce by the reaction would pass through the membrane, and the product is structurally and/or functionally different from the compound of interest; 5) The product is analyzed to determine whether the compound is suitable for use as a drug or natural product.

The specification disclosure does not sufficiently teach the presently claimed screening method because, firstly, the claimed screening method would require prior knowledge of the characteristics of both reactants (i.e. the biological material and the compound of interest) since the biological material must be of higher molecular weight than the known compound so that the biological material would not pass through the membrane. For example, if the biological material is a protein and the compound is a known drug, the claimed screening method would have required prior knowledge of the characteristics of both the protein and the known drug such that the protein has a higher molecular weight. The specification is directed to the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin (pg. 10, line 11 to pg. 11, line 2). The specification example 1 discloses the method of screening for the oxidized form of

chlorpromazine due to the hepatic cytochromes P450 oxidation of chlorpromazine. Example 2 discloses the method of screening for the oxidation product of pentoxyresorufin by cytochrome P450 2B-catalyzed O-dealkylation activity. Thus the specification does not sufficiently teach the relationship between biological materials and known compounds to use in the claimed high throughput screening method.

Secondly, since prior knowledge of both reactants in a reaction is required for the claimed screening method then the product of the reaction would also be known. Thus the claimed screening method is screening for a product that is already known, wherein its use would be apparent.

Thirdly, the claimed analyzing step requires the extrapolation of the resulting analyses of the reaction product to determine the use of the compound as a drug or natural product. The specification is silent on how the product is being analyzed in order to determine that the compound can be used as a drug or natural product. Thus the specification does not sufficiently teach how the product is being analyzed in order to determine that the known compound can be used as a drug or natural product.

The specification is directed to the screening method for the interaction of cytochromes P450 (biological material) and a drug (compound of interest), wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin. These methods clearly do not provide an adequate representation regarding the relationship between all biological materials and known compounds for the claimed screening method. The specification's examples are drawn specifically to the interaction of cytochromes P450 with the drug such as imipramine,

chlorpromazine, and pentoxyresorufin. Thus the specification does not teach the claimed high throughput screening method.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin disclosed by the specification, the skilled artisan cannot envision the method of screening that would require prior knowledge of the relationship between any reactants (i.e. the biological material and the compound) and the analysis step wherein the resulting analyses of the product of the reaction would determine the use of the compound as a drug or natural product. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification support the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin. The specification does not teach the presently claimed high throughput screening that would require prior knowledge of the relationship between any reactants (i.e. the biological material and the compound) and the analyses step wherein the resulting analyzes of the product of the reaction would determine the use of the compound as a drug or natural product. Therefore, only the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin, but not the full breadth of the claim method would meet the written description provision of 35 U.S.C 112, first paragraph, but not the full breadth of the presently claim high throughput screening method.

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 13-23, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

See MPEP § 2172.01. The omitted steps are: 1) the step of determining how the product is structurally and/or functionally different from the initial compound of the reaction. The step is required in order to provide a membrane that would only allow the "product" to pass through to form the second solution.

2) The step wherein the resulting analysis of the product of the reaction would determine the use of the compound as a drug or natural product. This step(s) is essential in order to extrapolate the analysis of the product to determine that the compound of interest can be use as a drug or natural product.

3) The step of analyzing the product of the reaction when the products are small molecules that are absorbed by the cell as claimed in claim 21. The step is required in order to provide a membrane that would only allow the "product" to pass through to form the second solution.

4) The step of extrapolating the concentrations of the small molecules to determine cellular permeability or absorption as claimed in claim 30 for the determination of the compound for use as a drug or a natural product. This step(s) is essential in order to extrapolate the analysis of the product to determine that the compound of interest can be use as a drug or natural product.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

21. Claims 13-22 are rejected under 35 U.S.C. 102(a) as being anticipated by van Breemen et al. (*Drug Metabolism and Disposition*, **2/1998**, 26(2):85-90).

> *The instant claim 13 recites a high throughput method for screening a compound of interest comprising the steps of 1) placing a solution of biological material that has a higher molecular weights than the compound of interest into an ultrafiltration chamber. The chamber comprises a membrane with a pore size that does not allow the biological material to pass through; 2) Placing the compound of interest into the ultrafiltration chamber, which comprises a membrane with a pore size that does allow passage of the compound; 3) Providing a continuous flow of a supportive solution to the ultrafiltration chamber that facilitates the reaction between the compound and biological material; 4) The product produce by the reaction would pass through the membrane, and the product is structurally and/or functionally different from the compound of interest; 5) The product is analyzed to determine whether the compound is suitable for use as a drug or natural product.*

Van Breemen et al. disclose the method of pulsed ultrafiltration-mass spectrometry for identifying drug metabolites formed by hepatic cytochromes P450 (Abstract; pg. 85, right col., line 10 to pg. 86, left col., line 15). The ultrafiltration chamber comprises a methylcellulose ultrafiltration membrane (refers to the membrane of the instant claim) with a pore size that allow for the drug metabolites to pass through (pg. 86, left col., lines 37-64). The method steps comprise loading the chamber with the cytochromes P450 microsomes (refers to the biological material of the instant claim), loading a mobile phase (refers to the supportive solution of the instant claims) of ammonium acetate, NADPH, drug (refers to the compound of interest of the instant claim) and buffer into the chamber, incubating the mixture to allow the drug to react with the microsomes (refers to the reaction step of the instant claim), and analyzing the product of the reaction (refers to the product of the reaction of the instant claim). The drug includes

imipramine, chlorpromazine, and pentoxyresorufin. Additionally, the method discloses aligning the chamber in parallel (refers to claim 22 of the instant claim) (pg. 89, left col., lines 6-11; fig. 3). Therefore, the method of van Breemen et al. clearly anticipates the presently claimed method.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
March 17, 2004

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600